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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/079,709	02/19/2002	Robert F.M. Van Gorcom	246152002603	9896

25225 7590 07/14/2004

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EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 07/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/079,709	VAN GORCOM ET AL.	
	Examiner	Art Unit	
	David J Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-47* is/are pending in the application.

4a) Of the above claim(s) *44-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-43 and 47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 November 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] Claims 32-47 are pending in the application.

Restriction/Election

[2] Applicants' election without traverse of the invention of Group I, claims 32-43 and 47, filed June 01, 2004, is acknowledged. The elected invention is drawn to a purified and isolated DNA that hybridizes to SEQ ID NO:25, a recombinant expression system, a recombinant vector, a recombinant microbial host cell, and a method of expressing a nucleotide sequence encoding a fungal phytase.

[3] Based upon the disclosure, it appears that a probe having the sequence of SEQ ID NO:25 was used to isolate the nucleic acid of SEQ ID NO:31 by hybridization. SEQ ID NO:25 is a degenerate probe, and at least one "species" of SEQ ID NO:25 binds to SEQ ID NO:31. It follows that, because SEQ ID NO:25 is a subsequence of SEQ ID NO:31, if SEQ ID NO:25 is allowable over the prior art, then SEQ ID NO:31 should also be allowable over the prior art. For the reasons stated above, the subject matter of Groups I and IV have been rejoined. It should be noted that the relationship of SEQ ID NO:25 to SEQ ID NO:31 is not expressly stated in the specification. Applicants are requested to verify the examiner's interpretation of this relationship.

[4] Claims 44-46 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim.

[5] Claims 32-43 and 47 are being examined only to the extent the claims read on the subject matter of Groups I and IV.

Priority

[6] Applicants' claim to domestic priority under 35 USC 121 to US non-provisional applications 09/233,510, 08/419,448, 08/151,574, and 07/688,578 in the preliminary amendment filed February 19, 2002 is acknowledged.

Information Disclosure Statement

[7] Applicants assert the references cited in the IDS filed August 12, 2002 have been filed in US non-provisional application 09/233,510. However, upon review of application 09/233,510, the examiner cannot locate the cited references. Thus, the information disclosure statement fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Drawings

[8] It is noted that applicants have provided sequence identifiers for sequences disclosed in the drawings in a preliminary amendment filed February 19, 2002. The drawings are objected to because it is unclear as to which sequence identifier

corresponds to the appropriate sequence. It is suggested that applicants clearly identify the sequence identifier that corresponds to a particular sequence. Appropriate correction is required.

[9] The drawings are objected to because Figures 2, 6, and 8 are not numbered in accordance with 37 CFR 1.84(u)(1). A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Oath/Declaration

[10] The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. The oath or declaration is defective because: 1) It does not state that the person making the oath or declaration acknowledges the duty to disclose to the Office all information known to the person to be material to patentability as defined in 37 CFR 1.56; 2) It does not state that the person making the oath or declaration believes the named inventor or inventors to be the original and first inventor or inventors of the subject matter which is claimed and for which a patent is sought; and 3) It does not state that the person making the oath or declaration has reviewed and understands the contents of the specification, including the claims, as amended by any amendment specifically referred to in the oath or declaration.

Specification/Informalities

[11] The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: -- Polynucleotide Encoding a Fungal Phytase --.

[12] The first paragraph of the specification is objected to as the status of nonprovisional parent application(s) 09/233,510 and 07/688,578 has not been listed. If a parent application has become a patent, the expression "now Patent No._____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

Claim Objections

[13] Claims 32 and 34 are objected to as reciting non-elected subject matter. It is suggested that, for example, applicants amend the claim such that it no longer recites non-elected subject matter.

[14] Claim 47 is objected to as being dependent upon a claim drawn to a non-elected invention. It is suggested that, for example, applicants amend the claim such that it no longer depends upon a non-elected claim. For purposes of examination, the claim has been examined as though the limitations of claim 44 were incorporated into the claim.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

[15] Claim(s) 32-43 and 47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

[a] Claim 32 (claims dependent therefrom), 34 (claims 35-43 dependent therefrom), and 47 are indefinite in the recitation of "hybridizing" as this term is unclear absent a statement of the conditions under which the hybridization reaction is preformed. Nucleic acids which will hybridize under some hybridization conditions will not necessarily hybridize under different conditions.

[b] Claims 36 and 37 (claim 38 dependent therefrom) are indefinite in the recitation of "18-amino acid AG leader sequence" (claim 36) and "AG promoter" (claim 37). It is unclear as to the nucleic acid sequence that is intended as being an "18-amino acid AG leader sequence" or an "AG promoter" and as such, it is unclear as to the scope of claimed expression systems. It is suggested that applicants identify the intended nucleic acid sequence encoding a "18-amino acid AG leader sequence" and an "AG promoter."

[c] Claims 39-42 are confusing as the art recognized meaning of the term "expression system" is a host cell that allows for expression when transformed with an appropriate expression vector. However, claims 39-42 are drawn to a host cell comprising an expression system, which has been interpreted as, in accordance with the art recognized meaning of the term "expression system," a host cell comprising a

host cell transfected with an expression vector. It is suggested that applicants clarify the meaning of the term.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

[16] Claims 32-43 and 47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of he claimed invention.

Claim 32 (claim 33 dependent therefrom) is drawn to a genus of DNAs encoding a fungal phytase that hybridize to SEQ ID NO:25. Claims 34 (claims 35-42 and 43 dependent therefrom) and 47 are drawn to a genus of recombinant expression systems encoding a fungal phytase comprising a nucleotide sequence that hybridize to SEQ ID NO:25. For claims drawn to a genus, MPEP § 2163 states the written description requirement for a genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or

disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. In this case, the specification discloses only a single representative species of the claimed or recited genus of DNAs or nucleic acids encoding a fungal phytase, i.e., a nucleic acid encoding SEQ ID NO:31. Other than this single species, the specification fails to disclose other representative species of the genus of claimed DNAs and expression systems.

Further, because of the wide variation within the sequence of SEQ ID NO:25 and that one of skill in the art would recognize that SEQ ID NO:25 is merely a minimal fragment of a larger encoding nucleic acid, the claims encompass species that are widely variant in structure. While one could argue that all species encompassed by the genus must possess this structural feature, it should be noted that this feature, being a minimal fragment of a larger nucleic acid, does not constitute a substantial portion of the genus.

Also, it is noted that the genus is limited to those DNAs that encode a "fungal phytase." MPEP § 2163 states (citing *Amgen*, 927 F.2d at 1206, 18 USPQ2d at 1021), "A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials". In this case, the specification fails to

provide those characteristics that distinguish a DNA encoding a "fungal phytase" from those DNAs that encode phytases that are not of fungal origin and thus fails to adequately describe the genus.

Therefore, given the lack of description of a representative number of compounds, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

[17] Claim(s) 32-43 and 47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid or recombinant expression vector encoding SEQ ID NO:33, does not reasonably provide enablement for all DNAs or recombinant expression vectors that hybridize to SEQ ID NO:25 or nucleotides 210-1715 of SEQ ID NO:31 and encode a fungal phytase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

It is the examiner's position that undue experimentation would be required for a skilled artisan to make and/or use the entire scope of the claimed invention. Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The

existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP § 2164.01(a). The Factors most relevant to the instant rejection are addressed in detail below.

- The claims are overly broad in scope: The claims are so broad as to encompass a vast number of nucleic acids encoding fungal phytases. The broad scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the number of nucleic acids broadly encompassed by the claims. In this case the disclosure is limited to a nucleic acid encoding SEQ ID NO:33.

- The lack of guidance and working examples: The specification provides only a single working example of the claimed polynucleotide, i.e., SEQ ID NO:31. This single working example fails to provide the necessary guidance for making the entire scope of polynucleotides. The specification fails to provide guidance regarding those nucleotides of SEQ ID NO:31 that may be altered by substitution, addition, insertion, and/or deletion with an expectation of maintaining the desired activity phytase.

- The high degree of unpredictability in the art: The nucleotide sequence of an encoding nucleic acid determines the corresponding encoded protein's structural and functional properties. Predictability of which changes can be tolerated in an encoded protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e., expectedly intolerant to

modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. The positions within an encoding nucleic acid's sequence where modifications can be made with a reasonable expectation of success in obtaining an encoded polypeptide having the desired activity/utility are limited in any protein and the result of such modifications is highly unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions. In this case, the necessary guidance has not been provided in the specification as explained in detail above. Thus, a skilled artisan would recognize the high degree of unpredictability that the entire scope of polynucleotides would encode a polypeptide having the desired activity. The ability to assign a protein's function based on similarities to other proteins, even those that are naturally occurring, is *highly* unpredictable.

- The state of the prior art supports the high degree of unpredictability: The state of the art provides evidence for the high degree of unpredictability in altering a polynucleotide sequence with an expectation that the encoded polypeptide will maintain the desired activity/utility. For example, Branden et al. ("Introduction to Protein Structure", Garland Publishing Inc., New York, 1991) teach "[p]rotein engineers frequently have been surprised by the range of effects caused by single mutations that they hoped would change only one specific and simple property in enzymes" and "[t]he often surprising results of such experiments reveal how little we know about the rules of protein stability... ...they also serve to emphasize how difficult it is to design *de novo* stable proteins with specific functions" (page 247). While it is acknowledged that this

reference was published in 1991, to date there remains no certain method for reasonably predicting the effects of even a *single* amino acid mutation on a protein. Such mutations may even completely alter a protein's activity. As a representative example, Witkowski et al. (*Biochemistry* 38:11643-11650) teaches that a single amino acid substitution results in conversion of the parent polypeptide's activity from a beta-ketoacyl synthase to a malonyl decarboxylase (see e.g., Table 1, page 11647). Thus, the prior art acknowledges the unpredictability of altering a protein-encoding sequence with an expectation of obtaining a protein having a desired function and discloses that even a single substitution in a polypeptide's amino acid sequence may completely alter the function of a polypeptide.

- The amount of experimentation required is undue: While methods of isolating variants of a given nucleic acid are known, e.g., hybridization, it is not routine in the art to screen for all DNAs having a substantial number of substitutions or modifications as encompassed by the instant claims.

Thus, in view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high degree of unpredictability, and the significant amount of experimentation required, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention. As such, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)).

Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections – Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

[18] Claims 32-43 and 47 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-24 of US Patent 6,350602 B1 (the "'602 Patent"). An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); and *In re Longi*, 759 F.2d 887, 225 USPQ 645

(Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 32-43 and 47 of the instant application are generic to all that is recited in claims 1-24 of the '602 Patent, i.e., claims 32-43 and 47 of the instant application are anticipated by claims 1-24 of the '602 Patent.

[19] Claims 32-43 and 47 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of US Patent 5,436,156 (the "'156 Patent"). An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); and *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 32-43 and 47 of the instant application are generic to all that is recited in claims 1-13 of the '156 Patent, i.e., claims 32-43 and 47 of the instant application are anticipated by claims 1-13 of the '156 Patent.

Conclusion

[20] Status of the claims:

- Claims 32-47 are pending.
- Claims 44-46 are withdrawn from consideration.
- Claims 32-43 and 47 are rejected.

- No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (571) 272-0942. The Examiner can normally be reached Monday-Friday from 7:00 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The FAX number for submission of official papers to Group 1600 is (703) 872-9306. Draft or informal FAX communications should be directed to (571) 273-0942. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

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Patent Examiner
Art Unit 1652
07-09-04